Worldwide Effort To Map the Bovine Genome

First there was the mapping of the human genome. Then, this spring, scientists announced they had nearly completed the genome mapping of the mouse. Now, scientists are in the early stages of mapping the bovine genome to help produce cattle with improved production traits and to possibly help in finding cures for human diseases.

The Agricultural Research Service is part of a group of government and university laboratories from four continents in the initial stages of mapping the bovine genome. The ARS research effort is led by Steven Kappes and John Keele of the Roman L. Hruska U.S. Meat Animal Research Center, in Clay Center, Nebraska. Kappes is center director, and Keele is an animal scientist.

The project began in spring 2000, when Kappes started contacting labs from around the world to develop a physical (bacterial artificial chromosome—BAC) map of cattle. Bacteria—and more specifically, bacterial chromosomes—are used as hosts for pieces of bovine chromosomes. The bacterial hosts are used to generate many identical copies of a piece, or clone, of cattle DNA. The BAC map will be a useful tool for identifying genes that affect production traits in farm animals and an excellent resource to improve the efficiency of a future effort to sequence the entire bovine genome.

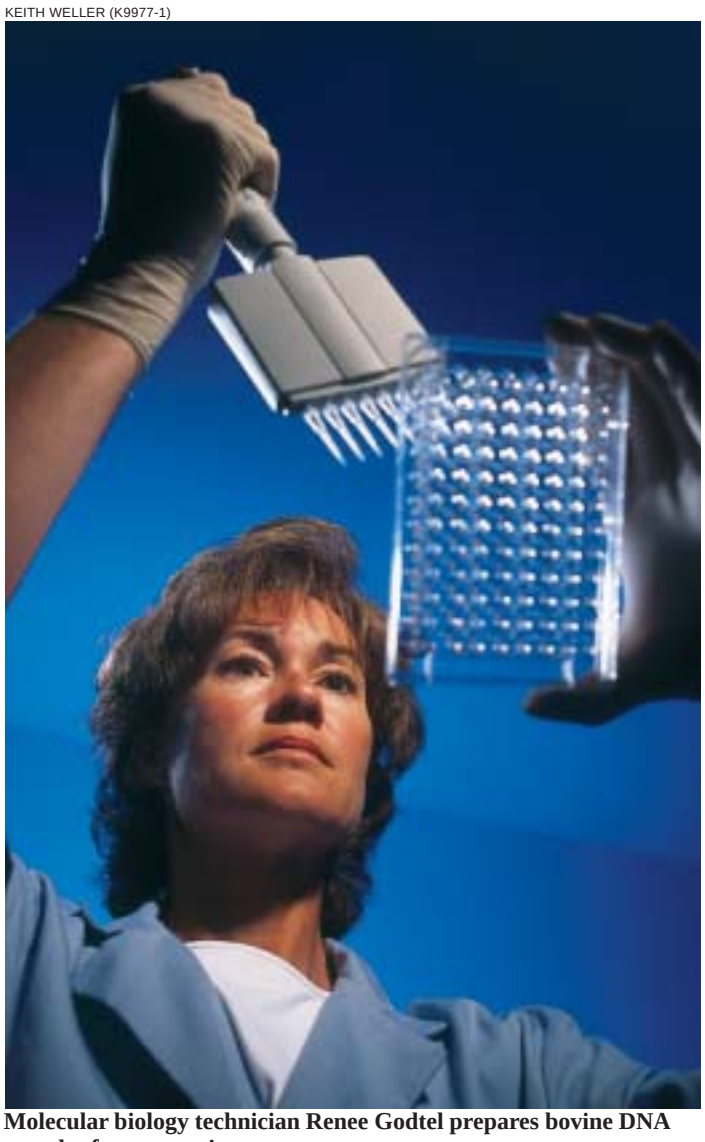
The first step in the process is to fingerprint individual BAC clones. Researchers at the British Columbia Cancer Agency Genome Sciences Centre have been funded to construct a fingerprinted BAC map. A fingerprint is obtained by cutting DNA from a BAC clone into pieces and separating the fragments on a gel. The fingerprint pattern of the different fragments is used to identify overlapping BAC clones. A BAC map is the collection of overlapping clones that represent the entire bovine genome.

Funding for this part of the project has been provided by USDA-ARS; the Biotechnology and Biological Sciences Research Council and Roslin Institute, from the United Kingdom; the University of Alberta and the Alberta Science and Research Authority, in Canada; and the University of Illinois.

The fingerprinting will be performed on 280,000 BAC clones from two libraries constructed by scientists at the Children's Hospital Oakland (California) Research Institute. The first BAC library was constructed from Holstein bull DNA and the second from Hereford bull DNA. Each BAC clone contains about 170,000 bases of cattle DNA.

The second step, which can occur simultaneously with fingerprinting, is sequencing both ends of all 280,000 clones. This work is being conducted by ARS, the University of Illinois, Texas A&M University, AgResearch of New Zealand, the Commonwealth Scientific and Industrial Research Organization of Australia, the Brazilian Agricultural Research Corporation, and the University of Alberta. The Institute of Genomic Research in Rockville, Maryland, has been contracted to do some of the sequencing. The National Institute for Agricultural Research in France is fingerprinting and end-sequencing clones

KEITH WELLER (K9977-1)



Molecular biology technician Renee Godtel prepares bovine DNA samples for sequencing.

from a BAC library constructed in their laboratory. They will combine their information later with the international effort. Kappes is talking with other organizations to help with the end sequencing.

The scientists will combine the end-sequencing and fingerprinting information to determine the overlapping BAC clones. Kappes says, "Ideally, we would like one set of contiguous overlapping clones—'contigs'—for each of the 30 chromosomes in the bovine genome. But it's likely that we'll have gaps between several contigs for each chromosome."

So far, 249,000 of the 280,000 cattle BAC clones have been fingerprinted, and the end-sequencing effort is under way. The completion date for the bovine BAC map is February 2003.

The researchers hope that the next phase of the project will be sequencing the bovine genome. Kappes and other scientists have sent a proposal to the National Institutes of Health (NIH) to do this work.

The BAC map alone costs $4.5 million, while NIH estimates it may cost $100 million to sequence the bovine genome to a finished stage. Kappes says the effort is expensive, but it will have many tangible benefits. Scientists from ARS and elsewhere will use the BAC map and sequence information to improve productivity traits in cattle. This means they may be able to more accurately select genetically superior animals for specific needs, such as lean beef, milk production, reduced feed requirements, and improved health and welfare. This ability would increase the profitability of beef production. The research should also benefit those who raise sheep, since the genetic makeup of sheep is very similar to that of cattle.

This research may also help the medical community. "As we define certain biological mechanisms in livestock, the information may benefit human medicine," says Kappes. "We are currently defining a genetic mechanism affecting muscling in sheep. This is of specific interest to research efforts in human medicine because a similar mechanism is observed in cancer cells."

Not only is there similarity in the DNA sequences of genes in farm animals and in humans, but also the biological processes are very similar across species. Eventually, researchers will be able to compare the human genome to the bovine genome to help determine the function of genes for both livestock production and human well-being.—By **David Elstein,** ARS.

This research is part of Food Animal Production, an ARS National Program (#101) described on the World Wide Web at http://www.nps.ars.usda.gov.

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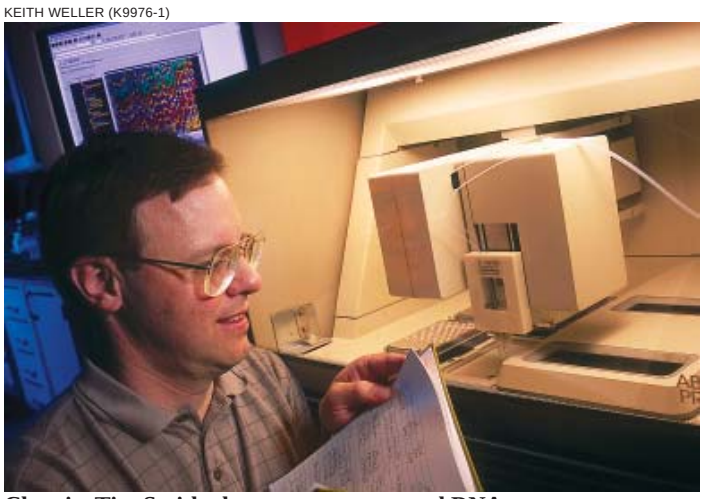
Along with the genomics group at MARC, animal scientist John Keele is part of the team that's working to produce a BAC map of the bovine genome.

KEITH WELLER (K9976-1)



Chemist Tim Smith observes an automated DNA sequence instrument, which produces 96 bovine DNA sequences every 3 hours.

DUANE SMAILUS (K9976-20)

At the British Columbia Cancer Agency Genome Sciences Center in Vancouver, Canada, genomics technologist Pawan Pandoh prepares BAC fingerprints used in creating the bovine map.